What is the relationship between whole grain intake and type 2 diabetes?

Conclusion

Consumption of whole grains is associated with a reduced incidence of type 2 diabetes in large prospective cohort studies.

Grade: Limited

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

Four articles met the inclusion criteria and were reviewed to determine the effect of whole grain consumption on the incidence of type 2 diabetes (T2D). Of the four papers, one was a systematic review and meta-analysis of six prospective cohorts, as well as a separate prospective cohort study (de Munter et al, 2007, positive quality); one was a systematic review of 12 studies (one RCT and 11 prospective cohort studies of which five were relevant to this question) (Priebe MG et al, 2008, positive quality); one was a RCT (Brownlee et al, 2010, neutral quality) and one was a prospective cohort study (Kochar et al 2008, neutral quality).

Both systematic reviews reported that whole grain intake was inversely associated with risk of T2D. They included a common sub-set of five prospective cohorts; one conducted a pooled analysis and the other did not. The systematic review and meta-analysis(de Munter et al, 2007) pooled the data of six prospective cohort studies (N=286,125 predominantly black and white male and female subjects with 10,944 incident cases of T2D) and found that a two-serving-per-day increment in whole grain consumption was associated with a 21% decrease in risk of T2D after adjustment for potential confounders and BMI (RR=0.79; 95% CI: 0.72, 0.87; P<0.001). Priebe 2008, reported on five prospective cohort studies that examined the effect of whole grain foods and found an inverse association ranging from 0.67 (95% CI; 0.32 to 1.38) to 0.79 (95% CI; 0.65 to 0.96). After excluding of studies that did not correct for family history of diabetes (Meyer 2000; Montonen 2003) and physical activity (Montonen 2003), the observed effect in the remaining three studies was a relative risk of 0.70, 0.73 and 0.73. Priebe 2008, also reviewed one RCT of low methodological quality, which reported that, in 12 obese hyperinsulinemic subjects, a six-week feeding intervention of whole grain foods at each meal compared to refined grain foods resulted in a slight improvement of insulin sensitivity (P<0.05).

Kochar et al, 2008 examined the association between cold ready-to-eat breakfast cereal consumption (whole grain and refined) and risk of T2D in a cohort of men from the Physicians' Health Study I (N=1,270 for cereal analyses). Incident T2D was determined from 19 years of annual follow-up questionnaires. Comparing the highest and lowest category of consumption, the relative risk for T2D was 0.63 (95% CI: 0.55, to 0.72; P<0.0001). The authors noted that their simplified food frequency questionnaire (FFQ) did not collect data that would allow them to control for total energy intake and other nutrients such as fiber and magnesium.

Brownlee IA et al, 2010 investigated the effect of substituting whole grain for refined grains on risk markers of insulin sensitivity. Subjects who routinely consumed few whole grain products were randomized to consume 60g whole grains per day for eight weeks or 60g whole grains per day for eight weeks and then 120g whole grains per day for eight more weeks. Self -reported whole grain intake by the ad libitum subjects was significantly increased in both intervention groups. No significant differences in marker of insulin sensitivity, serum glucose and insulin, were found between the control and the averaged intervention groups between groups.

Evidence Summary Paragraphs

Systematic Reviews

de Munter et al, 2007 (positive quality) a prospective cohort study, conducted in the United States, examined the associations between whole grain, bran, germ and risk of T2D. The authors examined this question further by conducting a systematic review and meta-analysis of six cohort studies. The prospective cohort included 161,737 women from the Nurses' Health Studies I (NHSI) (age 37-65 years) and II (26-46 years). Dietary intakes and potential confounders were assessed with regularly administered questionnaires during 12-18 years of follow-up. The median whole grain intake in the lowest and highest quintile of intake was 3.7

and 31.2 grams per day for NHSI and 6.2 and 39.9 grams per day for NHSII. After adjustment for potential confounders, the relative risks (RRs) comparing the extreme quintiles of consumption was was 0.63 (95% CI 0.57, 0.69) for NHSI and 0.68 (95% CI 0.57, 0.81) for NHSII (both: P<0.001). After further adjustment for body mass index (BMI), these RRs were 0.75 (95% CI 0.68, 0.83; >0.001) and 0.86 (95% CI 0.72, 1.02; >0.03), respectively. The associations for bran intake were similar to those for total whole grain intake. The association for germ intake after adjustment for bran was not significant.*Systematic review and Meta-analysis:* Prospective cohort studies on whole grain intake and risk of T2D were identified in searches of MEDLINE and EMBASE up to January 2007, and data were independently extracted by two reviewers. Based on pooled data for six cohort studies (conducted in the United States and Finland; the same five cohort studies as Priebe plus de Munter) including 286,125 predominantly black and white male and female subjects and 10,944 cases of type 2 diabetes, a two-serving-per-day increment in whole grain consumption was associated with a 21% (RR 0.79; 95% CI: 0.72, 0.87) decrease in risk of T2D after adjustment for potential confounders andBMI. Whole grain intake was inversely associated with risk of T2D. Additional analysis of whole grain components found that the association was stronger for bran than for germ.

Priebe MG et al, 2008 (positive quality) a Cochrane systematic review of studies conducted in Europe and the United States examined the effect of whole grain foods on prevention of type 2 diabetes (T2D). The literature search date range was all papers published prior to May 2006. Inclusion criteria forcohort studies was minimum duration of five years and evaluation of the relationship between whole-grain foods or cereal fiber intake and incidence of T2D. For RCT inclusion, the minimum study duration was six weeks and it had to assess the effect of a diet rich in whole-grain foods compared to a diet rich in refined grain foods on T2D and its major risk factors. One RCT and 11 prospective cohort studies met the inclusion criteria. Data were not pooled due to methodological differences. The one RCT studied 12 obese hyperinsulinemic subjects and found that a six-week feeding intervention of whole grain foods at each meal compared to refined grain foods at each meal resulted in a slight improvement of insulin sensitivity. Priebe et al obtained theinsulin sensitivity measurement finding from the authors (Pereira et al, 2002) as only the mean difference was reported in the publication. Insulin sensitivity (M-value) was measured with the euglycemic hyperinsulinemic clamp test and was significantly higher after the whole grain intervention compared to the refined grain intervention (P<0.05). The authors deemed the RCT to be of low methodological quality, as blinding and randomization were not described and the sample size was small.Of the 11 included prospective cohort studies, three examined whole grain intake, four studied cereal fiber intake, and two studied both. The five studies that examined the effect of whole grain foods consistently found an inverse association with T2D at the higher levels of consumption. The relative risks (RR) ranged between 0.67 (95% CI 0.32 to 1.38) and 0.79 (95% CI 0.65 to 0.96). After exclusion of studies that did not correct for family history of diabetes (Meyer 2000; Montonen 2003) and physical activity (Montonen 2003), the observed effect was very similar in the rest of the studies (RR of 0.70, 0.73 and 0.73). Overall, While the results of the cohort studies were homogenous, the authors stated that evidence from only prospective cohort trials was considered to be too weak to draw a definite conclusion about the effect of whole grain foods on the development of T2D.

Primary Studies

Brownlee et al, 2010 (neutral quality) an RCT, conducted in the United Kingdom, investigated the effect of substituting whole grain for refined grains on CVD risk markers. Subjects (N=266; BMI>25kg/m^2) who routinely consumed few whole grain products were randomized to consume 60g whole grains per day for eight weeks or 60g whole grains per day for eight weeks and then 120 g whole grains per day for eight more weeks. Markers of CVD risk and insulin sensitivity (BMI, percent body fat, waist circumference; fasting plasma lipid profile, glucose and insulin) were measured at baseline, eight and 16 weeks. A random intercepts model with time and whole grain intake factors was used to assess differences between the control and the average of the two intervention groups. Self-reported whole grain intake was significantly increased in both intervention groups. No significant differences in markers of insulin sensitivity were found between the control and the averaged intervention groups between groups.

Kochar et al, 2007 (neutral quality) prospective cohort study, conducted in the United States, examined the association between cold ready-to-eat breakfast cereal consumption (whole grain and refined) and risk of type 2 diabetes (T2D) in men from the Physicians' Health Study I (N=1,270 for cereal analyses). Cereal consumption was estimated using an abbreviated food questionnaire. Incident T2D was determined from 19 years of annual follow-up questionnaires. The median whole grain breakfast cereal intake in the lowest and highest category of intake was zero and at least seven cups per week, respectively. Comparing the highest and lowest category of consumption, the relative risk for T2D was 0.63 (95% CI: 0.55, to 0.72; P<0.0001). A limitation noted by the authors was that the simple food questionnaire for collection of dietary information did not allow controlling for total energy intake and other nutrients such as fiber and magnesium. Additionally, the study examined only one source of grain consumption; cold (ready-to-eat) breakfast cereals.

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Author, Year,	Participants,	Description of Study	Outcomes	Whole Grain

Study Design, Class, Rating	Duration, and Location	Design		Definition
Brownlee IA, Moore C et al, 2010 Study Design: Randomized controlled trial Class: A Rating:	N=266 participants. Age: 18-65 years. BMI>25kg/m^2. Consuming<30g WG per day . Location: United Kingdom.	Examined effect of substituting whole grain for refined grains on CVD risk markers using random intercepts model. Interventions: Control (no dietary Δ). Int 1: 60g WG per day x 16 weeks. Int 2: 60g WG per day x eight weeks, then 120g WG per day for eight weeks. Measures taken at zero, eight and 16 weeks. Whole-grain foods were provided; intake data was self-reported on EPIC FFQ.	Dropout rates: WG Int 1=19% WG Int 2=23% Control=6%. WG Int 1 and 2 outcome measures were averaged and then compared to controls. There were no significant differences in any markers of insulin sensitivity between the combined intervention groups and the control.	Selected whole grain foods were provided to free-living subjects.
deMunter JSL, Hu FB et al, 2007 Study Design: Prospective cohort study; Meta-analysis Class: M Rating:	*Meta-analysis* N=286,125 subjects and 10,944 cases of type 2 diabetes from six cohort studies including this one. Cohorts included predominantly white or black populations of men and women. Locations: United States and Finland. *Prospective Cohort Study* N=161,737 women; 73,327 from Nurse's Health Study I (NHSI)	Pooled meta-analysis of six prospective cohort studies. For each study, the RR of T2D was expressed per two serving per day increment of whole grain intake (40g). Examined association between quintiles of whole grain consumption and incidence of T2D using Cox proportional hazards analysis to estimate RR. Used whole grain food composition database to directly calculate each participant's whole grain intake in grams per day. Used National Diabetes Data Group criteria for diagnosis of T2D.	A 40g ↑ in daily whole grain intake associated with a 21% ↓ in T2D risk; RR=0.79 (95% CI=0.72, 0.87) after adjustment for potential confounders and BMI. *Note: Pooled analysis did not include fiber.* RR highest vs. lowest quintile of whole grain intake: NHSI (Q5=31.2g per day) RR=0.63 (95% CI=0.57, 0.69) NHSII (Q5=39.3g per day) RR=0.68 (95% CI 0.57, 0.81) (both: P<0.001); adjusted for potential confounders. RR after further	20 grams whole grain defined as one serving. For the study by Montonen, one serving was defined as 30 grams of grain. Intact and pulverized forms of whole grain containing the expected proportion of bran, germ and endosperm for the specific grain types. The following ingredients in the database were considered whole. Grains: Whole wheat and whole wheat flour, whole oats and whole oat flour, whole cornmeal and whole corn flour, brown rice and brown rice flour, whole rye and whole rye flour, whole barley, bulgur, buckwheat, popcorn, amaranth and psyllium.

	Baseline Ages=37-65 years; starting with 1984 FFQ. 88,410 from NHSII; Baseline age=26-46 years, starting with 1991 FFQ. Duration: NHSI-18 year follow up; NHSII-12 year follow up. Location: United States.		adjustment for BMI: NHSI=0.75 (95% CI 0.68, 0.83; P<0.001) NHSII=0.86 (95% CI 0.72, 1.02; P=0.03). *Note: Associations for bran intake were similar to those for whole grain intake, association for germ intake after adjustment for bran was not significant.*	
Kochar J, Djousse L et al, 2007 Study Design: Prospective cohort study Class: B Rating:	N=21,152 males from the Physicians Health Study I. For the whole-grain vs. refined grain analysis, N=17,270 as 3,882 subjects were excluded for failing to specify cereal brand. Baseline age: 39.7-85.9 years (1981-1983). Duration: 19 years. Location: United States.	Consumption of cold breakfast cereals estimated using abbreviated food questionnaire. Participants reported average consumption of cold breakfast cereals (by one-cup increments) during the past year. Hot cereal consumption (e.g. oatmeal) was not assessed.	Adjusted RR of T2D was 0.63 (95% CI=0.55, 0.72) for the highest category of cold whole-grain breakfast cereal consumption (at least seven cups per week) (P for trend <0.0001). Distribution for total, whole and refined grain was skewed to the right, thus a gradient of consumption was used rather than quintiles. *Note: Fiber not a variable. Authors discussed a number of potential mechanisms for effect.*	Used algorithm developed by Jacobs et al, AJCN 1998 to classify breakfast cereals in to whole or refined grain. Cereals containing at least 25% of oat or bran were classified as whole grain.
Priebe MG et al 2008 Study Design: Systematic Review Class: M Rating:	The literature search included studies published prior to May 2006. 12 studies met the inclusion criteria: 11 prospective cohort studies (minimum duration of five years); five of these examined the effect of whole grain. One RCT (minimum duration of each intervention arm was six weeks). N=12 obese hyperinsulinemic subjects. Study	Examined the effect of whole grain foods on prevention of type 2 diabetes (T2D). Five prospective cohort studies examined the effect of whole grain foods. The RCT examined the effect of a diet rich in whole-grain foods compared to a diet rich in refined grain foods on T2D and its major risk factors. Data were not pooled due to methodological differences.	Five cohort studies found an inverse association with T2D and whole grain consumption: RR=0.67 (95% CI 0.32 to 1.38) to 0.79 (95% CI 0.65 to 0.96). Following exclusion of studies that did not correct for family history of diabetes (Meyer 2000; Montonen 2003) and physical activity (Montonen 2003), the observed effect in the remaining thee studies was similar RR=0.70, 0.73 and 0.73). RCT: Insulin sensitivity (M-value) measured with euglycemic hyperinsulinemic clamp test: Whole grain	Whole grain food was defined in most studies (Fung 2002; Liu 2000; Liu 2003; Meyer 2000) according to Jacobs et al (Jacobs 1998) and Liu et al (Liu 1999) and included dark bread, popcorn, cooked oatmeal, wheat germ, brown rice, bran and other grains (e.g. bulgar, kasha, couscous). Breakfast cereals were classified as whole grain if they contained more than 25% whole grain or bran. Montonen et al, 2003, modified this classification and did not include wheat germ and bran. Koh-Banerjee et al, 2004, converted reported amounts of whole grain foods to grams of whole grain per

	locations: Europe and the US.		test. Whole grain intervention (0.396 x 10-4±0.131 x 10-4mmol/kg/one minute; 1 per pmol/L) Refined grain intervention (0.323 x 10-4±0.043 x 10-4mmol/kg/one minute; 1 per pmol/L) Mean difference: 0.07 x 10-4mmol/kg/one minute; 1 per mmol/L, 95% CI 0.003 x 10-4 to 0.144 x 10-4; P<0.05). *Note: Findings for cereal fiber were similar to whole grain.*	day and also used the FDA definition for products eligible for a whole-grain health claim: Foods that contain more than 51% of whole grain (all portions of the kernel) per reference amount customarily consumed (FDA 2005). Van Dam et al, 2006, included "dark breads, such as wheat, rye, pumpernickel" and "high fibre, bran or granola cereals, shredded wheat" as whole grains.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

Brownlee IA, Moore C, Chatfield M, Richardson DP, Ashby P, Kuznesof SA, Jebb SA, Seal CJ. Markers of cardiovascular risk are not changed by increased whole-grain intake: The WHOLEheart study, a randomised, controlled dietary intervention. *Br J Nutr.* 2010 Mar 23: 1-10.

de Munter JSL, Hu FB, Spiegelman D, Franz M, van Dam RM. Whole grain, bran and germ intake and risk of type 2 diabetes: A prospective cohort study and systematic review. *PLoS Med* 2007; 4 (8): e261.

Kochar J, Djousse L, Gaziano JM. Breakfast cereals and risk of type 2 diabetes in the Physician's Health Study I. *Obesity.* 2007; 15 (12): 3,039-3,044.

Priebe MG, van Binsbergen JJ, de Vos R, Vonk RJ. Whole grain foods for the prevention of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2008 Jan 23;(1):CD006061.